Popular Article

Avian Influenza Understanding the Emergence of Bird flu in Livestock

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Abstract

Avian influenza (AI)have high pathogenicity (HPAI), causing severe systemic disease with multiple organ failure and high mortality rates. The fact that influenza A mainly spared bovines is particularly interesting, considering that over the past few decades, the majority of domesticated and wild animals and birds at the human-animal interface have perished from infection. Before the novel influenza D virus (IDV) recently surfaced in cattle worldwide, the evolution and host adaptation of influenza A virus (IAV) in this species faced significant obstacles, despite a few natural cases in the mid-1900s and seroprevalence of human, swine, and avian influenza viruses in bovines. It has been suggested that several bovine host factors, including some serum components and secretory proteins, have anti-influenza capabilities. This may help explain why bovines are resistant to IAV. The foundation of agriculture and food production is domestic cattle, whose roles are still vital in the contemporary world. Nonetheless, there exist disparities in the production and consumption of meat and milk in the various nations of the world, as well as in the distribution of cattle. The highly pathogenic avian influenza H5N1 strain spread from cattle to humans raising fears of the risks of a wider transmission of this virus from cattle to humans.

Keywords: Highly pathogenic avian influenza (HPAI), Hemagglutinin, Vaccination, Public Awareness, Cattle, H5N1

Introduction

Bird flu is a viral infection that affects primarily domestic poultry and pet, zoo, and wild birds. In domestic poultry, AI viruses are typically of low pathogenicity (LPAI), causing subclinical infections, respiratory disease, or decreased egg production. A few AI viruses, however, have high pathogenicity (HPAI), causing severe systemic disease with multiple organ failure and high mortality rates. The form of the disease resulting from HPAI viruses has historically been called fowl plague or fowl pest. Contrary to popular belief, humans and cattle do not naturally share a vulnerability to bidirectional influenza transmission. This poses a lot of questions, many of which do not yet have obvious solutions. Are influenza A viruses able to infect cattle? Why, in spite of the influenza A virus's rapid evolution, mutational robustness, and broad host ecology, did ruminants escape infection? What became of the influenza A viruses linked to cattle that first appeared in the early 1970s? Whether the virus overcame or avoided the host immunological selection pressure particular to its species. Japan published the first report on influenza in cows in 1949; however, no IAV with a cattle origin was found in these outbreaks. A number of bovine influenza pandemics and influenza-like respiratory illnesses were also seen in cattle during human pandemics. Around this time, strains were identified from several locations in Russia and Europe. While some of these strains differed from human IAV, others shared HA and NA glycoproteins that are comparable to the typical human H2 and H3 subtypes. The cattle influenza epidemic had a brief duration, lasting only two to three days, and the symptoms reported were fever (40–42 °C), blepharitis, nasal discharge, anorexia, tympanites, pneumonia, joint issues, and decreased lactation. This occurred in the fall of 1889 and 1893, as well as a few smaller epidemics that occurred in Japan between 1914 and 1916.Pigs have been the animals that combine human and avian influenza. At the pig–human interface, a virus and the association of humans with swine promoted the bidirectional transmission of influenza. It's interesting to note that humans have tamed cattle around 10,500 years ago whereas pigs were domesticated 9000 years ago. The highly pathogenic avian influenza (HPAI) H5N1 strain has been infecting cattle in a number of U.S. states. Three cases of human infection in dairy farm workers have also been reported for the first time, which has raised concerns about the possibility of a wider spread of this virus from cattle to humans. Since April, 19 locations in the Keralan districts of Alappuzha, Kottayam, and Pathanamthitta - where wetlands, migratory birds, poultry, and integrated farms are all part of the ecosystem- have reported H5N1 outbreaks. However, worries that the virus could spread widely have arisen as a result of the large-scale crow deaths in Alappuzha and the subsequent identification of the H5N1 virus in their carcasses.

The first case of probable mammal-to-human transmission of the HPAI A(H5N1) virus was confirmed by the CDC on April 1st, 2024, in a person who had been exposed to presumed-to-be-infected dairy cows in Texas. This is believed to be the first documented case of the virus in humans. Thirty-one herds in Colorado, sixty in Idaho, twenty-seven in Michigan, twenty-four in Texas, thirteen in Iowa, nine in Minnesota, eight in New Mexico, seven in South Dakota, four in Kansas, two in Oklahoma, and one in each of North Carolina, Ohio, and Wyoming have been found to have contracted the avian influenza virus type A (H5N1). In locations where the avian influenza virus type A (H5N1) has also been detected in dairy cattle, at least 35 cats have tested positive for the virus thus far. The sickness has apparently been severe in cats, a species previously known to catch the virus, presenting with neurological symptoms, copious oculonasal discharge, and a high fatality rate. These results highlight how crucial it is to keep pets away from rodents, wild birds, raw milk, and colostrum. When working in close proximity to cats that have been proven or suspected to have been exposed to HPAI, the CDC encourages veterinary professionals to take measures. The only symptoms observed in dairy farm laborers were eye redness, which is typical of conjunctivitis, and coughing without a fever in one individual. Together with more common flu symptoms including fever, chills, coughing, and sore throat/runny nose, poultry workers also experienced conjunctivitis. The CDC, which has been keeping a careful eye on the matter, guarantees that there is no evidence of person-to-person transmission and that these individual cases are unrelated to one another. Moreover, there hasn't been a rise in flu incidence among people. The CDC still believes that there is little danger of HPAI to the general public, based on the information that is currently available.

Avian influenza can kill entire flocks of birds so this causes devastating losses for the farming sector, Dr. Keith Hamilton, Head of the WOAH Preparedness and Resilience Department.

Etiology

Avian influenza viruses are type Aorthomyxoviruses (*Alpha influenza virus* or *Influenza virus A*) characterized by antigenically homologous nucleoprotein and matrix protein, which are identified by serological testing such as agar gel immunodiffusion (AGID) or ELISA. AI viruses are further divided into 16 hemagglutinin (H1–H16) and 9 neuraminidase (N1–N9) subtypes. Within each hemagglutinin subtype there may be additional sub classifications, such as distinct virus lineages, genetic clades and genotypes. From 1959 through May 2024, 46 distinct virus lineages caused HPAI outbreaks or events.

Synonyms: Bird flu, fowl pest, fowl plague, avian influenza A, highly pathogenic avian influenza disease (HPAI)

Pathogenesis of Bird flu

The pathogenesis of avian influenza involves a complex interplay between the virus, the host's immune response, and various environmental factors. Avian influenza can kill entire flocks of birds so this causes devastating losses for the farming sector, Dr. Keith Hamilton, Head of the WOAH Preparedness and Resilience Department.

1. Viral Entry and Initial Infection

The avian influenza virus typically enters the host through the respiratory or gastrointestinal tract. The primary modes of transmission include:

- Inhalation of Aerosols: The virus can be inhaled through contaminated dust or droplets.
- Ingestion: Birds may ingest the virus from contaminated water or food.

The virus attaches to host cells via its hemagglutinin (HA) protein, which binds to sialic acid receptors on the surface of epithelial cells in the respiratory and gastrointestinal tracts.

2. Replication and Spread

inside the host cell, the viral RNA is released into the cytoplasm and transported to the nucleus. Here, it hijacks the host's cellular machinery to replicate and produce new viral particles. The key steps include:

- Transcription and Replication: The viral RNA is transcribed and replicated. New viral proteins and RNA segments are produced.
- Assembly: New viral particles are assembled in the cytoplasm.
- Budding and Release: The newly formed viruses bud off from the host cell, acquiring a portion of the host cell membrane. The neuraminidase (NA) protein helps in the release of new viral

particles by cleaving sialic acid residues, preventing the clumping of virions.

3. Local and Systemic Spread

- Respiratory Tract: In low pathogenic avian influenza (LPAI) infections, the virus tends to remain localized in the respiratory tract, causing mild respiratory symptoms. In highly pathogenic avian influenza (HPAI) infections, the virus can cause severe damage to the respiratory epithelium, leading to significant respiratory distress.
- Gastrointestinal Tract: The virus can infect and replicate in the intestinal epithelium, particularly in waterfowl, leading to viral shedding in feces and further environmental contamination.
- Systemic Spread: In HPAI infections, the virus can breach the epithelial barriers and enter the bloodstream (viremia), spreading to multiple organs. The systemic spread can result in widespread tissue damage and high mortality.
- The spread of avian influenza from birds to people typically occurs occasionally and under particular circumstances.
- The risk of contracting avian influenza increases in people who have frequent or close contact with infected animals or extensively contaminated surroundings.

4. Immune Response and Pathological Changes

The host's immune response to avian influenza involves both innate and adaptive immunity:

- Innate Immunity: The initial response involves the activation of pattern recognition receptors (PRRs) like toll-like receptors (TLRs), which recognize viral components and trigger the release of cytokines and interferons. This response aims to limit viral replication and spread.
- Adaptive Immunity: The adaptive immune response involves the activation of T cells and B cells. Cytotoxic T cells target and destroy infected cells, while B cells produce antibodies that neutralize the virus.

5. Clinical Manifestations

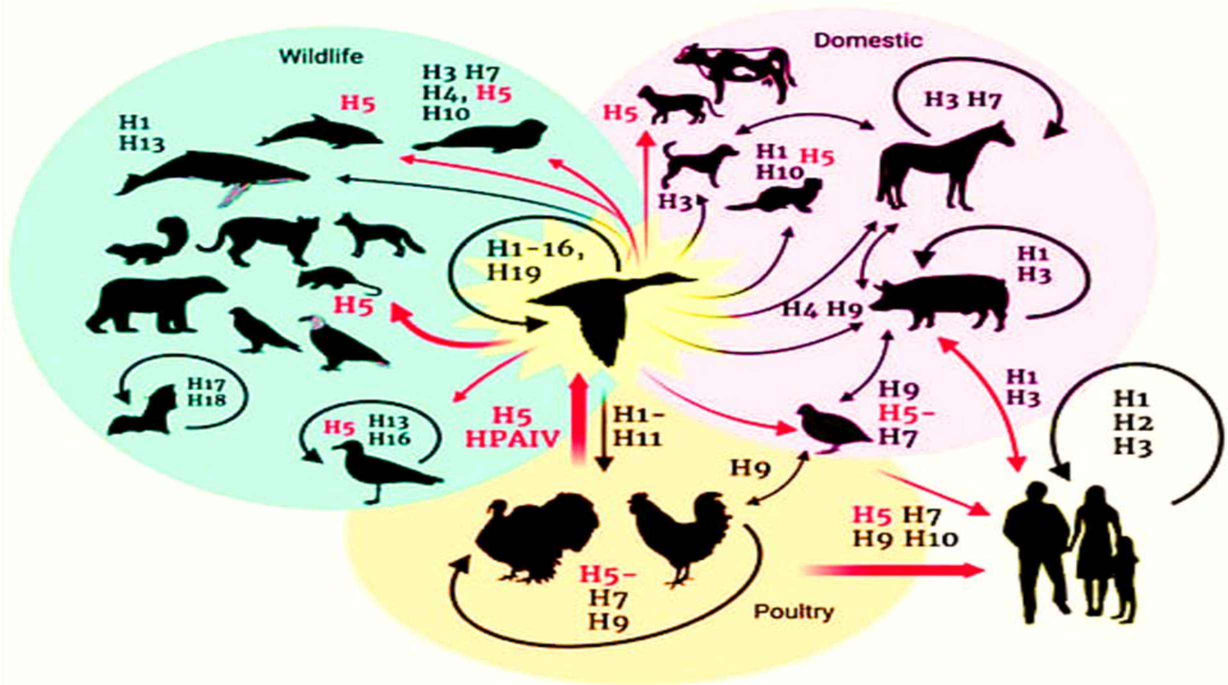
The clinical signs of avian influenza depend on the pathogenicity of the virus and the species of bird infected:

- LPAI: Birds may exhibit mild respiratory symptoms, such as coughing, sneezing, and nasal discharge, along with decreased egg production and mild systemic illness.
- HPAI: Birds may show severe symptoms, including sudden death, respiratory distress, swelling of the head, neck, and eyes, cyanosis of combs and wattles, hemorrhages on the skin and internal organs, diarrhea, and neurological signs like tremors and paralysis.
- Avian influenza can have a serious negative effect on the health of wild and poultry birds due to its high fatality rates. Oftentimes viewed primarily as disease carriers, wild birds including those of endangered species also suffer from the illness. The effects of avian influenza on wildlife have the potential to have a catastrophic impact on our ecosystems' biodiversity

Swollen and cyanotic face, wattle and comb

Subcutaneous haemorrhages in feet and shank

Severe haemorrhages in the ovaries



Avian influenza transmission flow from the natural reservoir (aquatic birds) to poultry, Bovine, Humans, and other animal species (Courtesy Giulia Graziosi 2024**)**

6. Pathological Findings

Post-mortem examinations of birds infected with HPAI viruses typically reveal:

- Respiratory Tract Lesions: Congestion, hemorrhages, and necrosis in the trachea, bronchi, and lungs.
- Gastrointestinal Lesions: Hemorrhages and necrosis in the intestines.
- Multiorgan Involvement: Lesions in the liver, spleen, kidneys, heart, and brain due to systemic spread.

Influenza A in Bovines

Haptoglobin and neutrophil counts were high in the blood in the majority of these instances. Paired sera from five cattle herds with identical clinical histories were screened serologically for *IBR, PI3, BRSV, adenovirus, M. bovis, H. somnus, C.*

psittaci, C. brunetti, and other viruses. All herds of *P. hemolytica, P. trehalosi*, and *P. treponemes* showed antibodies against BRSV and PI3. Only a few herds have BVD and IBR identified. That being said, these cattle sera showed notably elevated antibody titer to two human IAVs: 60% for A/England/333/80 (H1N1) and 65% forH3N2, A/England/427/88 just 5% of the cows had negative serotypes for both viruses. The exposure and natural susceptibility of cattle to human influenza A viruses will be provide these information. HPAI H5N1 has been naturally isolated from a diverse range of other animal species, including cats, dogs, foxes, seals, leopards, mustelidae (minks and otters), skunks, tigers, lions, pikas, otters, polecats, porpoises, raccoons, raccoon dogs, pigs, Virginia opossums, civets, badgers, bears, dolphins, stone/beech martens, coyotes, and even fish, This expanded range of hosts increases the potential for the virus to persist, evolve, and potentially cross species barriers, posing a threat to both animal and human health.

Diagnosis of Avian Influenza

Diagnosing avian influenza involves several laboratory tests and procedures:

1. *Virus Isolation and Identification*: Swabs from the trachea, oropharynx, or cloaca are collected and inoculated into embryonated chicken eggs or cell cultures. The presence of the virus is confirmed through hemagglutination and hemagglutination inhibition tests.

2. *Molecular Techniques*: Reverse transcription polymerase chain reaction (RT-PCR) is used to detect viral RNA in clinical samples. This method is highly sensitive and specific, allowing for the rapid identification of avian influenza subtypes.

3. *Serological Tests*: Enzyme-linked immunosorbent assay (ELISA) and agar gel immunodiffusion (AGID) tests are used to detect antibodies against avian influenza viruses in the blood of infected birds.

Current status of Bird flu in India

India has witnessed several outbreaks of avian influenza over the past decades, with the most recent ones occurring in 2021 and 2022. These outbreaks have affected various states, leading to the culling of thousands of poultry birds to prevent the spread of the disease.

On 18thApril 2024a H5N1 outbreak was detected in ducks in two parts in Alappuzha district, Kerala. The disease was confirmed in a lab for ducks reared in the area. The District Collector has decided to initiate the process of culling domestic birds within a 1 kilometre radius from the epicentre of the outbreak. As of May 9, district officials have culled 60,232 birds in Alappuzha. Farmers were compensated 100 per ducklings and chicks, 200 per older bird, and 5 per egg destroyed. A four-year-old child from West Bengal was diagnosed with bird flu in late January this year, was admitted to a hospital’s intensive care unit for treatment twice for acute respiratory distress and was discharged finally in May, according to the World Health Organisation.

The Indian government, through the Department of Animal Husbandry and Dairying, has implemented strict measures to control and prevent avian influenza. These measures include:

- **Surveillance and Monitoring**: Regular monitoring of bird populations, especially in high-risk areas, to detect early signs of the disease.

➢ **Rapid Response**: Immediate culling of infected and exposed birds, disposal of carcasses, and decontamination of affected areas.

➢ **Public Awareness**: Educating poultry farmers and the general public about biosecurity measures and the importance of reporting suspected cases.

➢ **Vaccination**: While not commonly used, vaccination of poultry against avian influenza is considered in certain high-risk situations.

➢ Despite these efforts, the threat of avian influenza remains due to the constant movement of migratory birds, which can carry the virus across borders. Continued vigilance and cooperation between government agencies, poultry industries, and the public are essential to keep this deadly disease at bay.

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